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Feature
Book Review

Genesis of *What Is Life?*: A Paradigm Shift in Genetics History

Review of: *Creating a Physical Biology: The Three-Man Paper and Early Molecular Biology*, edited by Phillip R. Sloan and Brandon Fogel; 2011; 319 pp; University of Chicago Press (Chicago); ISBN-13: 978-0-226-76783-3

Reviewed by John R. Jungck, Departments of Biological Sciences and Mathematical Sciences, University of Delaware, Newark, DE 19716

Most geneticists can easily name a dozen papers that transformed their field. Many of these papers continue to be reprinted and commented upon by historians, philosophers, literary critics, science technology and society scholars, and biologists. Such papers include Mendel's 1866 plant hybridization paper; Sutton's 1902 synthesis of Mendel with meiosis, which thereby coupled chromosomal mechanics with independent assortment; Morgan's 1910 paper on sex linkage; Wright's 1930 "Evolution in Mendelian Populations"; Luria and Delbrück's 1942 paper on the fluctuation test; and, of course, Watson and Crick's 1953 paper on the structure of DNA. A seminal piece that is often absent from these lists is *What Is Life?: The Physical Aspect of the Living Cell*, in which Erwin Schrödinger (1944) offers his interpretation of the "Three-Man Paper" (3MP). The three men who authored the 3MP in its original German, "Über die Natur der Genmutation und der Genstruktur," were Nikolai Timofeéff-Ressovsky, Karl Zimmer, and Max Delbrück. While Delbrück, a theoretical physicist, went on to win a Nobel Prize for his later work with Salvador Luria, the other two authors were of equal stature in their fields of experimental genetics and experimental radiology. Schrödinger's book, rather than the original 3MP, has caught the attention of many geneticists, who argue that it prompted physicists to move into biology after World War II and instigated the hunt for an "aperiodic crystal" and a "code script" that many felt led to the discovery that DNA was the hereditary molecule and the deciphering of the genetic code.

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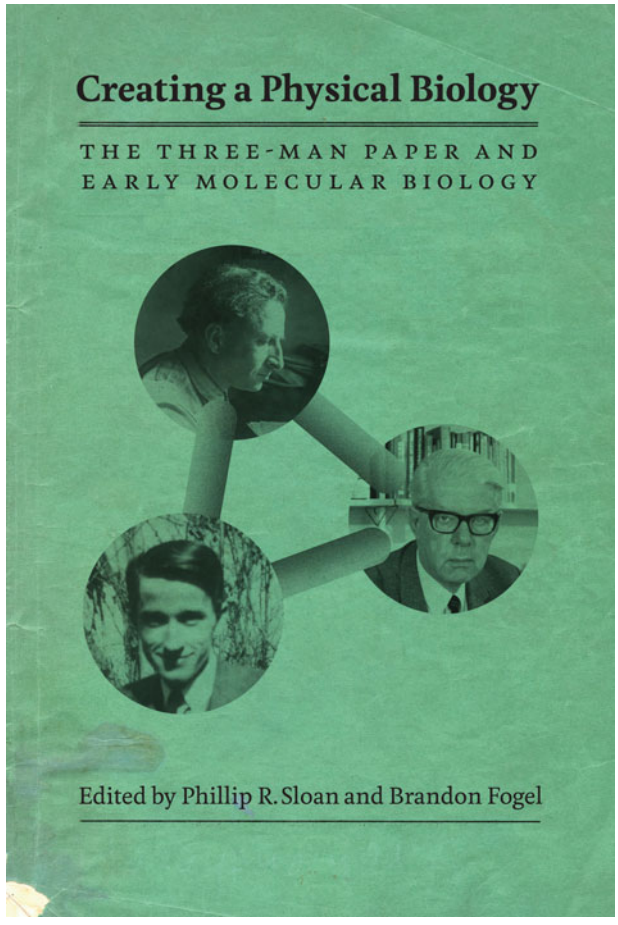
Address correspondence to: John R. Jungck (jpoley@gsu.edu).

Creating a Physical Biology is a collection by a series of authors who return to the source—situating the 3MP in its own historical period. Well-prefaced and edited by Sloan and Fogel, the essays in this collection highlight the differences



between the actual 3MP and Schrödinger's text. They relate the 3MP to issues of teleology and reductionism, especially whether physicists like Bohr really expected biology to have fundamental new physical laws. They also summarize mechanistic conceptions of life, various misreadings of the paper, and the development of biophysics. In my view, the treatment of these topics reinforces the importance of interdisciplinarity, theory construction, and careful mathematical analysis, as well as the value of collaboration among workers from different educational backgrounds.

The collection includes Fogel's extraordinarily readable English translation of the 3MP (pp. 221–271). I urge readers to read this first to get a sense of the prescience of this seminal paper and to then read the "Translator's Preface" (pp. 214–220). This will avoid a "prefiltering" (Sankaran, 2012) by the commentators and translator and afford the treat of seeing Timofeéff-Ressovsky's clever experiments to determine the impact of x-rays in inducing mutations by making use of Nobel laureate Hermann J. Muller's "C1B" and "attached X" crossing methods for identifying mutants in *Drosophila melanogaster.* Timofeéff-Ressovsky's experiments investigated mutation rates as a function of x-ray dosage, wavelength, and temperature. He also distinguished spontaneous from induced mutations, concluding that induced mutations only affected one of the two alleles and that some mutations were reversible. In the second section of the paper, Zimmer articulates the famous "target theory," which posited a set of simplifying assumptions that accounted for the probabilistic interaction between radiation and the target (genes). Delbrück then synthesizes much of the preceding experimental work and uses analogies from quantum mechanical thinking to make interpretations about the nature of genes. He concludes that genes are macromolecules with a specific atomic composition ("a well-defined assemblage of atoms") that can be altered by x-radiation and states, "We want to emphasize that the fundamental property of the gene [is] its identical self-replication during mitosis . . ." Finally, all three coauthor the final section of the article to draw their general conclusions: "The genome is a highly complicated physical-chemical structure, consisting of a series of specific, chemical pieces of matter—the individual genes.. . . it leads to an explicit or implicit critique of the cell theory; the cell, thus far from proving itself so magnificently as the unit of life, dissolves into the 'ultimate units of life,' the genes." Wow! I had no idea that such language and specificity preceded Schrödinger. I am embarrassed that I never investigated the antecedent before.

Michael A. Goldman (2011) says: "Sloan and Fogel argue that Schrödinger's *What Is Life?* misrepresents the 3MP. They note, for instance, that he misleads by saying that quantum mechanics makes possible 'a complete reduction of biological to physical systems,' which the paper never claims. Schrödinger also ignores its reservations about mapping genotype to phenotype. But there is little evidence that he intended to provide an authentic account." Because Schrödinger's *What Is Life?* is so responsible for most geneticists' understanding of the 3MP, such re-examination of its claims is important.

An important addition to this wonderful collection is the work of Alexander von Schwerin (2010), who gives a detailed reappreciation of the target theory. Furthermore, he helps us appreciate the transition in our thinking over the past century: He puts the 3MP into further context by tracing the subsequent history of approaches to understanding mutagenesis. In particular, he notes that Charlotte Auerbach, in 1969, substantially changed our view of mutagenesis from being an aberrant chemical or physical (x-ray) damage to being a normal biological process. "It is a task of its own to draw that historic line of 'physiologization' of mutations—and, hence, of the activation of the organism as an actor of its own in the process of the transformation of external stimuli into mutations." With Miroslav Radman's work on trade-offs between accuracy and efficacy, which led to a resolution of the neo-Lamarckians' attack on Darwinism with their adaptive mutation hypothesis by showing demonstrably that the rate of production of mutations due to mismatch repair systems or fidelity of DNA replication is related to the harshness and/or stability of a population's environment, this important distinction becomes all the more important.

Was the 3MP crucial to a paradigm shift? The wonderful translation and commentary provided by *Creating a Physical Biology* has convinced me that it did. Furthermore, while the "target theory" turned out to be incorrect, the synthetic research program laid out a heuristic approach to future practice and set an extraordinarily high standard for the synthesis of experiment, theory, and mathematical hypothesis testing. Furthermore, *Creating a Physical Biology* offers insight into a moment in time when such a substantial shift in thinking occurred and speculation on why and how it did.

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